

REMARKS

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow. Claim 18 is requested to be cancelled. Claims 1, 17 and 19 are currently being amended.

After amending the claims as set forth above, claims 1-17 and 19-23 are now pending in this application. This amendment adds, changes and/or deletes claims in this application. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claim(s) remain under examination in the application, is presented, with an appropriate defined status identifier.

The amendment of claim 1 is supported by the application as originally filed, does not add new matter, and is otherwise proper. Support for the amendment to claim 1 may be found throughout the specification but particularly in paragraphs [0052] and [0058]. Specifically, claim 1 has been amended to change the phrase “immobilizing a nucleic acid or a protein on a solid support” to “immobilizing a nucleic acid or a protein within a solid support.” Claim 17 has also been amended to change the phrase “immobilizing a nucleic acid or a protein on a solid support” to “immobilizing a nucleic acid or a protein within a solid support.” This amendment to claim 17 also finds support in specification paragraphs [0052] and [0058]. Claim 17 has been further amended to add the phrase “repeating steps (a) through (c) one or more times. This amendment is supported by originally filed claim 18. Claim 19 has been amended to depend from claim 17. Applicants respectfully request entry of these amendments in their entirety. In view of the above amendments and following remarks, applicants respectfully request reconsideration of the claims and submits that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

CLAIMS

I. Rejection of Claims under 35 USC § 102

A. Wang et al. (U.S. Patent 5,922,617)

Applicants respectfully traverse the rejection of claims 1-4, 7-14, 17-19, and 21 as purportedly anticipated by Wang et al. (U.S. Patent 5,922,617). A prima facie case of anticipation under 35 USC § 102 requires that a single reference teach each and every element of the claimed invention. The present invention as defined, e.g., by amended claim 1 distinguishes over the cited reference by reciting a nucleic acid or protein immobilized within a solid support. Because the Wang reference simply does not teach this element, it fails to disclose each and every element of the claimed invention.

The present invention differs significantly from the cited reference. The Office Action states that Wang et al. “teach a method for characterizing a nucleic acid-protein interaction or a protein-protein interaction, comprising immobilizing a nucleic acid or a protein on a solid support...” However, a closer reading of Wang et al. reveals that the nucleic acids and/or proteins are immobilized on the surface of the solid substrate (see, e.g., Wang et al. column 3, line 39; col. 7, lines 3-4). Webster’s dictionary defines a “surface” as “the exterior or upper boundary of an object or body” (Merriam Webster’s Collegiate Dictionary 10th ed. 1997, page enclosed). Thus, the Wang et al. patent discloses that the nucleic acids and/or proteins are placed on the external portion of a magnetic bead or a circular disc. At no point do Wang et al. teach or suggest that the nucleic acids and/or proteins are immobilized within the solid substrate.

This distinction between the claimed invention and that of Wang has real world consequences. Because immobilization within a support, as opposed to immobilization on a support, naturally employs an additional dimension (depth), it provides the advantage of far greater capacity for immobilization (Specification paragraph [0022]). The immobilization technique of Wang et al., confined to the surface of the solid support, lacks this important advantage.

Because Wang et al. do not teach any method using a nucleic acid and/or protein bound within a solid substrate, Wang et al. fails to teach each and every element of the claimed invention. Therefore, the Wang reference does not anticipate claim 1 or claim 17 of the present

invention, and it cannot anticipate claims 2-4, 7-14, and 19, which depend either from independent claim 1 or independent claim 17. Claim 18 has been cancelled and therefore the rejection of claim 18 is rendered moot. Accordingly, applicants respectfully request that the Examiner withdraw the rejection of claims 1-4, 7-14, 17 and 19.

B. Guschin et al.

Applicants respectfully traverse the rejection of claims 17, 20 and 21 as allegedly anticipated by Guschin et al. (*Analytical Biochemistry*, 250: 203-211 (1997)). The present invention as defined, e.g., by amended independent claim 17 distinguishes over the cited reference at least by repeating the basic immobilization and assay steps. By contrast Guschin fails to disclose this element and therefore fails to teach each and every element of the claimed method. Guschin therefore cannot anticipate claim 17. Likewise, claim 20 and claim 21, which depend from claim 17, cannot be anticipated. Accordingly, applicants respectfully request the Examiner withdraw the 35 U.S.C. § 102 rejection based on Guschin et al.

II. Rejection of Claims under 35 U.S.C. § 103(a)

A. Drobyshev et al.

Applicants respectfully traverse the rejection of claim 5 and claim 6 as being allegedly unpatentable under 35 U.S.C. § 103 over Drobyshev et al. (*Nucleic Acids Research*, 27: 4100-4105 (1999)). As stated in § 2143 of the MPEP,

[t]o establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

Applicants respectfully submit that a prima facie case of obviousness has not been established.

First, the Office Action has failed to set forth how the prior art teaches each element of the claimed methods. Applicants submit that claim 5 and claim 6 distinguish over the cited reference by reciting immobilizing a protein within a solid support, contacting the nucleic

acid and the protein under conditions which allow the nucleic acid and the protein to interact, and measuring the strength of the nucleic acid-protein interaction. On its own, Drobyshev et al. teaches only the use of a gel pad to study an interaction between DNA and a synthetic dye; it does not teach the interaction between DNA and protein, thus, it fails to teach any of the elements of independent claim 1 from which claim 4 and claim 5 depend. By contrast, as the Examiner admits, Drobyshev et al. "does not teach wherein a nucleic acid-protein interaction is analyzed via a gel pad(s)." Thus, as no other reference has been cited, only through modification may the reference make the current claims obvious.

It is respectfully submitted that there is no suggestion either in Drobyshev or in the knowledge generally available to one of ordinary skill in the art to modify the Drobyshev reference to provide for DNA-protein interactions in which one of the molecules is immobilized within a solid support. Applicants respectfully disagree with the Examiner's assertions that Drobyshev provides motivation to modify the reference. The Office Action states that

the reference provides motivation for [nucleic acid-protein interaction]. The reference teaches the use of gel pads as an immobilization support in oligonucleotide, DNA and protein arrays provides essential advantages over the use of probes attached to a solid support. The reference states that three-dimensional immobilization in gel pads provide higher capacity and a more homogeneous environment than heterophase immobilization on glass or filters.

However, this is nothing more than an obvious to try rationale.

Here, "what was 'obvious to try' was to explore a new technology or general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it." MPEP § 2145, X.B. (emphasis added). The teachings of Drobyshev, and specifically the statement that "immobilization in gel pads provides higher capacity and a more homogeneous environment" is nothing more than an "invitation" to experiment because this statement does not provide sufficient guidance or specificity as to how to execute that plan. The issue is not whether it is obvious that gel pad immobilization techniques can generally be used to provide higher capacity and a more homogenous environment. Rather, the issue is whether it is obvious to modify a technique involving a small molecule dye and DNA on gel pads to produce a gel pad assay for an interaction between nucleic acids and protein.

As stated in § 2144.03 of the MPEP, “it is never appropriate to rely solely on ‘common knowledge’ in the art without evidentiary support in the record, as the principal evidence upon which a rejection was based.” In this case, the Office Action simply fails to provide evidence that one skilled in the art would modify the Drobyshev reference. Applicants respectfully request that by either official notice or a piece of prior art, the Examiner support the statement that one of skill in the art would modify the Drobyshev reference to obtain the present invention.

Finally, the Examiner fails to show that one of ordinary skill in the art would have a reasonable expectation of success in modifying the teachings of Drobyshev to produce the current invention. Whether the claimed methods are obvious depends on more than whether gel pads provide “higher capacity and a more homogenous environment.” As shown in Drobyshev these advantages worked well when measuring the interaction between a permanent DNA binding dye and DNA; however, there is no suggestion in Drobyshev that these would still constitute advantages when studying the interaction between DNA and proteins.

Bisbenzimidazole, the component dye of Hoescht differs drastically from protein. The dye’s small size allows it to bind to immobilized DNA without cross hybridization or high background. One simply cannot assume that an interaction found to exist between a large biological molecule and a small synthetic molecule is predictive of conditions “which allow [a] nucleic acid and [a] protein to interact.” Proteins vary greatly, with some proteins binding to double stranded DNA, some proteins binding to single stranded DNA, some proteins binding to other nucleic acids, and many proteins not binding to DNA at all. These functional differences exist in addition to differences found in size, amino acid composition, charge, and the like. Assuming that a technique which successfully works with a small non-protein dye to study DNA-protein interactions can be extended to study protein-nucleic acid interactions is tenuous at best. As one of skill in the art would understand, use of the technique in Drobyshev could have just as easily resulted in impermissible levels of background and impermissible requirements for protein concentrations as resulting in the advantages of the present invention.

For the reasons set forth above, applicants respectfully submit that a prima facie case of obvious has not been met with respect to claim 5 and claim 6. Therefore, applicants respectfully request the Examiner withdraw this ground of rejection and allow the claims to issue.

B. Wang et al. in view of Ahern et al.

Applicants respectfully traverse the rejection of claims 15, 16, 22 and 23 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Wang et al. in view of Ahern. As noted in section 2143 of the MPEP to establish a prima facie case of obviousness, the references when combined, must teach or suggest all the claim limitations. As stated in the discussion of the Wang reference above, Wang fails to disclose a biological molecule embedded within a solid support. The Ahern reference, a description of kits containing simple pre-made reagents, fails to cure this deficiency. Moreover, the Examiner has pointed to no suggestion or motivation to modify either reference to supply the missing element. Therefore, applicants respectfully assert that a prima facie case of obviousness regarding claims 15, 16, 22, and 23 has not been met. For this reason, applicants respectfully request the Examiner withdraw the rejection and allow the claims to issue.

CONCLUSION

For the foregoing reasons, applicants respectfully assert that the application is now in a condition for allowance. Consequently, applicants respectfully request the Examiner withdraw all of the rejections and allow the application to issue. The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

Respectfully submitted,

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